

May 2, 1998

Patrea L. Pabst  
Arnall Golden & Gregory, LLP  
2800 One Atlantic Center  
1201 West Peachtree Street  
Atlanta, Georgia 30309-3450

Re: LEN 101 "Method and Compositions for Treatment of Cancers"

Dear Mrs. Pabst:

Thank you for your draft of the above titled patent application. As per your letter of April 30, 1998, I will attempt to respond herein to your request for additional information as described on pages 8&11 of the application.

Page 8, para beginning line 16 might read: " This procedure has been demonstrated to cause a significant response (greater than 50% reduction in size of tumors) in a variety of solid tumors in approximately 50% of patients who have failed all other treatment modalities. In metastatic melanoma clinical trials, a tumor specific inflammatory response provoked by ultrapheresis has been documented in approximately 75% of patients. This inflammation is characterized by redness, swelling, warmth, and tenderness and is confined to tumors only. There has been no associated injury to non-cancerous tissue. This tumor specific inflammatory response has led to a 50% or greater reduction in the size of tumors in 50% of patients studied so far. Clinical trials have also demonstrated a 44% major reduction of tumor metastases in human breast cancer, and prostate cancer. Insufficient clinical data exists to claim response rates in other tumor types but tumor specific inflammation has been observed in patients with metastatic colon cancer, ovarian cancer, lung cancer, head and neck cancer, cervical and endometrial cancers. In some cases this inflammation has been followed by significant tumor regressions in each tumor type. The significance of response in such diverse tumor types, strongly suggests that ultrapheresis modifies the patients response to the tumor in favor of successful immunologic control of the tumor.

## Page 11 "Examples"

Mrs J.R. is a 44 year old lady who had metastatic breast cancer that had failed radiation therapy and the drugs; cytoxan, adriamycin, 5-FU, taxol, cis-platin, navabine, tamoxifen and arimedes. Tumor at the time of ultrapheresis was documented in lungs, bone and skin of the entire left anterior and lateral chest. She was treated with 15 ultrapheresis procedures over a three week period. She experienced marked inflammation in the tumors in her skin, increased pain from the tumors in her bones, and swelling of the tumors in her lungs. She then received the drug thalidomide 200mg at night. The redness and swelling in her skin improved within 2 days and her breathing returned to normal within one week. Two weeks after completing treatment.

then

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all tumor in her skin had resolved clinically, her bone pain resolved and the tumors in her lungs resolved on repeat CAT scan. One week latter she returned to work as a school counselor. She is to all testing disease free two months after treatment and is being monitored closely on thalidomide at the same dose.


Mr. P.G. is a 54 year old engineer with metastatic melanoma with metastases to lung and to lymph nodes in the mediastinum. He received 24 ultrapheresis procedures resulting in a 25% reduction of tumors. He was subsequently treated with an additional 12 procedures resulting in minor tumor reduction despite evidence of tumor inflammation. The tumors regrew within one month. He was again retreated with ultrapheresis again resulting in inflammation and some minor regression but then received thalidomide at the time of tumor inflammation. Two months latter repeat CAT scan showed complete disappearance of tumors in the lung and mediastinum. He is being followed closely and shows no evidence of disease 6 months after completing treatment and has no medical complaints.

Mrs. J.K. is a 43 year old lady with metastatic leiomyosarcoma with six (6) lung metastases all of which developed within one month of surgery on both lungs to remove tumors. these tumors had also failed methotrexate, adriamycin, ifosphomide, and dactinomycin. She received 24 ultrapheresis procedures with no side effects. One month later CAT scan revealed only four (4) tumors and these were reduced in size by 50%.

Dr. R.S. is a 59 year old gentleman with metastatic adenocarcinoma of the left upper lung with metastases to liver, brain and bones. His tumors had failed to respond to taxol, cis-platin and etoposide. His brain tumors had responded to radiation therapy. He received 15 ultrapheresis procedures. Each procedure caused increased pain in tumors of his spine, pelvis, right hip and left shoulder. Follow up scans after ultrapheresis treatment revealed resolution of tumors in pelvis, spine, hip, and ribs. There was a 50% reduction in the primary tumor in the lung and liver. Thalidomide was then started at 200mg each night. One month latter the scans revealed further reduction in the tumors in lung and liver. The patient's pains have all resolved, he is asymptomatic.

I hope this information is helpful. If you need any additional information please call or we can use email. My address is [rlentz@bellsouth.net](mailto:rlentz@bellsouth.net). Thank you again for your good work, I am

Sincerely yours,

  
M. Rigdon Lentz M.D.